REMARKS

Claims 1-13 remain pending in the present application.

1. ***Improper Final Rejection***

Initially, Applicants traverse the finality of the outstanding Office Action, which the Examiner indicates was necessitated by Applicants' amendment submitted November 19, 2008 (outstanding Office Action, page 6).

Applicants direct the Examiner's attention to the Office Action issued August 19, 2008, wherein the Examiner made a number of formal rejections, and recommended that Applicants amend claim 1 to "indicate a composition of tranilast" (page 3, last line).

Accordingly, Applicants respectfully submit that the amendment was made in order to address formal matters only, and that the Examiner was aware of and had fully searched and considered the subject matter of the claims in their amended form. In support of their contention, Applicants quote the Examiner from page 10 of the previous Office Action:

> Claim 1 is directed to method for the inhibition of post-operative adhesion formation in an internal body cavity, the method comprises administering tranilast or an analog thereof, directly onto said tissue surfaces in said body cavity. Therapeutically effective amount of the tranilast or analog thereof is administered to inhibit the adhesion.
>
> To expedite examination of the claims, the claim is examined as administering a composition containing tranilast or analog of tranilast present in an effective amount to inhibit the adhesion. (Emphasis added).

As such, the Examiner's change in the nature of the prior art rejection was not necessitated by Applicants' amendment, and the outstanding Office Action should not have been made final. Withdrawal of the finality of the outstanding Office Action is requested.

2. ***Incomplete Office Action***

In Applicants' previous response of November 19, 2008, Applicants directed the Examiner's attention to the unexpected results obtained by using the claimed compositions (see page 13 of previous response, re-asserted below).

The Examiner has failed to consider these results, which provide a rebuttal to any *prima facie* case of obviousness as to the present claims. No reference is made in the outstanding, Final Office Action, as to these results. It is respectfully submitted that the Examiner is not at liberty to ignore evidence of unexpected results.

As such, Applicants submit that the outstanding Office Action is incomplete **37 C.F.R. 1.104(b)**. A new non-final Office Action and restart of the statutory period is requested on this basis.

Rejection under 35 U.S.C. 103 over Adachi et al.
in view of Hubbell et al.

Claims 1-5 and 7-13 are rejected under 35 U.S.C. §103(a) as obvious over Adachi et al. in view of Hubbell et al. Applicants traverse this basis for rejection and respectfully request reconsideration and withdrawal thereof.

Adachi et al. is discussed at length in the present specification at page 5, lines 6-26 (identified as "Shinya et al."), wherein Applicants indicate that the

authors administered Tranilast orally both pre- and post-operatively in a rat intraperitoneal adhesion model.

Adachi et al. fail to disclose or suggest "...locally administering a composition comprising a delivery vehicle containing Tranilast, or an analog thereof, directly onto said tissue surfaces at the surgical site..." as is required by claim 1.

The Examiner cites Adachi et al. for the proposition that

> Adachi discloses administration of tranilast that inhibits adhesion, post operatively and preoperatively; administration is oral and the recitation of systemic in claims 12 and 13 reads on oral; tranilast is administered melted and in combination with carboxymethyl cellulose sodium (left column 52, first full paragraph) so that Adachi meets the delivery vehicle of claims 1-3; the recitation of "amounts ... effective to inhibit formation of adhesion" represents any amount deemed effective by the artisan so that that requirement of claims 1 and 5; Adachi administers 60 mg/kg/per day, pre and post operatively, thus meeting claim 11; the recitation that the barrier is absorbable is a property of the barrier so that the teaching of Adachi that the tranilast is administered with the cellulose derivative, carboxymethyl cellulose sodium; meets the limitation of the barrier and thus meets claim 4; Adachi discloses that it is well known in the art that tranilast is effective drug for bronchial asthma, atopic dermatitis, allergic rhinitis, decreasing granulation, inhibit collagen synthesis of human cheloid tissue transplanted onto the backs of mice (page 52, under materials and methods); regarding claims 8-10, it is noted that Adachi teaches single dose per day administration and Adachi's silence on burst or sustained release of tranilast reflects an inherent teaching of either mode of release and the forms of release recited in claims 9 and 10 would flow from the composition that is administered and since Adachi administers the same composition as the claimed invention, it flows that the release of Adachi's formulation when administered meets the claimed release in claims 9 and 10. Regarding claim 7, one drug analog can be used in place of the other with the expectation of providing inhibitory effect on adhesions. Adachi teaches administration of composition containing tranilast to treat

> postoperative adhesions. Adachi does not administer the composition directly to surgical sites. (Final Office Action, pages 3-4; emphasis added).

Notably, the Examiner's recitation is almost entirely silent as to how Adachi et al. is relevant to claim 1, which requires local administration of Tranilast in amounts effective to inhibit formations of adhesions. Likewise, Adachi et al. is silent in this regard, as recognized by the Examiner at the bottom of the paragraph.

The Examiner attempts to cure the deficiencies of Adachi et al. with Hubble et al.

> But Hubbell teaches that surgical adhesions such as post surgical adhesions are preventable or treated by topical administration of compositions comprising agents that inhibit adhesions (abstract; column 3, line 64 to column 4, line 14; claims 1-16). In Hubbell, the agents are hirudin, ancord and others column 4, lines 23-33, claims 1-16). While the agents of Hubbell are not tranilast, the teachings of Hubbell and Adachi both show tranilast (Adachi), ancord and hirudin (Hubbell) as agents that inhibit adhesion. (Final Office Action, page 4; emphasis added).

Hubble et al. disclose a method of preventing adhesions by topical administration of fibrinolysis enhancing agents, such as urokinase, tPA, hirudin or ancrod (abstract). As recognized by the Examiner, Tranilast is not among the fibrinolysis agents disclosed by Hubble et al.

As to fibrinolysis agents, Hubble et al. state:

> These agents all work by activation of the enzyme plasminogen, causing it to lyse fibrin. Other substances investigated for removal or prevention of fibrin strands have included proteolytic enzymes, drugs and clotting inhibitors such as heparin, which tend to prevent

> deposition of additional fibrin, referred to herein as "fibrinolysis enhancing agents". (Col. 2, lines 1-7).

There is no evidence in either of Hubble et al. or Adachi et al. that Tranilast is effective as a fibrinolysis agent and therefore a suitable substitute for the fibrinolysis enhancing agents of Hubble et al.

Accordingly, the skilled artisan would have had no reasonable expectation of success in inhibiting adhesions via topical application of Tranilast, derivable from the cited references. As stated above, Hubble et al. suggests fibrinolysis agents for topical administration. Withdrawal of the rejection is requested.

In drawing a conclusion of obviousness in the combination of Adachi et al. and Hubble et al., the Examiner states:

> Therefore, taking the teachings of Adachi and Hubbell, one having ordinary skill in the art at the time the invention was made would have the option to topically or orally administer the agent for inhibiting or treating or preventing postoperative adhesion or surgical adhesion and expect that topical or oral administration of the agent would effectively inhibit of prevent surgical or postoperative adhesions. (Final Office Action, page 4; emphasis added).

Applicants submit that the Examiner's argument is merely an impermissible hindsight reconstruction of the present claims, based upon a reading of the present specification. There is nothing in Adachi et al. to suggest that Tranilast would be effective for inhibiting adhesions upon topical administration. In fact, Applicants have even demonstrated that Tranilast via oral administration is ineffective for inhibition of adhesions (Example 3 and Tables 14 and 15, pp. 33-37 of specification), contrary to Adachi et al.'s disclosure.

Likewise, the Examiner is engaging in a leap of faith that one truly skilled in the art would not take, i.e. that a drug which is effective via one route of administration would necessarily be effective via a different route of administration. Applicants submit that this is nonsense. Would the skilled artisan consider it obvious to orally administer a drug which is known to be effective for topical administration? No. Withdrawal of the rejection is requested on this basis.

Rejection under 35 U.S.C. 103 over Adachi et al.
in view of Hubbell et al. and further in view of Sheffield et al.

Claims 1-13 are rejected under 35 U.S.C. §103(a) as obvious over Adachi et al. in view of Hubbell et al. and further in view of Sheffield et al. Applicants traverse this basis for rejection and respectfully request reconsideration and withdrawal thereof.

Applicants reiterate their comments in traverse of the combination of Adachi et al. and Hubbell et al. as applied to the present claims, set forth above.

Sheffield et al. disclose topical administration of non-steroidal anti-inflammatory drugs (NSAIDS) to the site of a surgical trauma to avoid post-surgical adhesions.

Sheffield et al. fail to disclose or suggest Tranilast as an NSAID, and cannot therefore cure the deficiencies of the combination of Adachi et al. and Hubbell et al. as applied to claim 1, as discussed above. (Applicants recognize that Sheffield et al. is cited only as to claim 6, but must demonstrate that it fails to cure the underlying deficiencies of the combination of primary and secondary references.)

Withdrawal of the rejection for failure to establish a *prima facie* case of obviousness is requested.

Unexpected Results

The Examiner is also requested to consider the data presented in the present application, which Applicants believe indicates unexpected results over the closest prior art of Adachi et al.

Applicants questioned the validity of the Adachi et al. study for various reasons (page 5, lines 14-16 and 23-26). Review of the data in Example 3 (pp. 33-34; and Tables 14 and 15 of the specification) reveals that oral administration of Tranilast is ineffective in preventing post-surgical adhesion, contrary to the suggestions of Adachi et al. The remaining examples demonstrate the efficacy of local administration of Tranilast compositions to post-surgical sites in preventing adhesions.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Account No. 50-2478 (14924).

In view of the foregoing, it is respectfully submitted that the present claims are in condition for allowance. Prompt notification of allowance is respectfully solicited.

If the Examiner has any questions or wishes to discuss this application,

the Examiner is invited to contact the undersigned representative at the number set forth below.

Respectfully submitted,

Date: May 26, 2009

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